Behavioural Science Section / Viewpoint

Gerontology

Gerontology 2012;58:545–553
DOI: 10.1159/000341157

Received: April 16, 2012
Accepted: June 20, 2012
Published online: August 16, 2012

Looking for 'System Integrity' in Cognitive Epidemiology

Ian J. Deary

Centre for Cognitive Ageing and Cognitive Epidemiology, Department of Psychology, University of Edinburgh, Edinburgh, UK

Key Words
Cognitive epidemiology · Common cause hypothesis · Illness and death · Intelligence and health · System integrity · System integrity hypothesis

Abstract
Background: In the last decade, an increasing body of empirical evidence has gathered to establish an association between higher cognitive ability in youth and later mortality, less morbidity and better health. This field of research is known as cognitive epidemiology. The causes of these associations are not understood. ***Objective:*** Among the possible explanations for the associations is the suggestion that they might, in part, be accounted for by general bodily 'system integrity'. That is, scoring well on cognitive ability tests might be an indicator of a more general tendency for complex systems in the body to be efficient. The construct of system integrity is critically assessed. ***Method:*** This viewpoint provides a critical presentation and an empirical and theoretical evaluation of the construct of system integrity as it is used in cognitive epidemiology. ***Results:*** A precedent of the system integrity suggestion is discovered. The empirical tests of the system integrity idea to date are critically evaluated. Other possible routes to testing system integrity are suggested. There is a critical re-evaluation of the idea and other, related concepts. ***Conclusion:*** The construct of system integrity is distinct from related constructs. It is still underdeveloped theoretically, and undertested empirically within cognitive epidemiology.

Cognitive Epidemiology: Intelligence and Health, Illness and Death

It is commonplace in research to inquire after the contributions that health and illness – and even impending death – make to individual differences in cognitive functioning, but asking about the reverse has only happened to any great extent in the last decade or so. The field of cognitive epidemiology studies the associations and mechanisms between prior cognitive functioning and health, illness and death through the life course. At its most longitudinal, it asks about the association between childhood cognitive ability and survival to old age.

The associations are now well established: higher cognitive ability in youth – whether that is childhood or young adulthood – is associated with living longer in studies addressing all-cause mortality [1]. Looking with-

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

0304–324X/12/0586–0545$38.00/0

Accessible online at:
www.karger.com/ger

Ian J. Deary
Centre for Cognitive Ageing and Cognitive Epidemiology
Department of Psychology, University of Edinburgh
7 George Square, Edinburgh EH8 9JZ (UK)
Tel. +44 131 650 3452, E-Mail i.deary@ed.ac.uk

in causes of mortality, higher cognitive ability in youth is associated with a lower likelihood of dying from, for example, cardiovascular disease, accidents, suicide, homicide, and other causes [2]. The evidence from cancer is less clear. The associations are not straightforwardly explained by cognitive ability tests being surrogates for childhood or own social class, or education [1, 2].

Causal Explanations in Cognitive Epidemiology

When we first found the association between childhood intelligence and survival, we made an attempt at suggesting mechanisms for the association [3]. Among these it was generally suggested that these could, 'include genetic factors, environment before and after birth …'. This does not exclude much. More specifically, four non-exclusive possibilities were listed and discussed. These asked the questions: What variance is childhood IQ picking up that might be related to subsequent health? What variance is it tapping that could be associated with mortality differences many years later? It was suggested that childhood IQ might be: a 'record of prior bodily insults'; a 'predictor of healthy behaviours', and a 'predictor of entry to safer environments'. The first of these views childhood intelligence as a statistical mediator between prior causes of health and eventual survival. The latter two view intelligence as a predictor and prior cause to other factors that are the more proximal causes of differences in health and mortality.

The fourth suggestion was the one that is the focus of this viewpoint, viz. *'Childhood IQ as an indicator of system integrity* – Childhood IQ might also act as a general, moderately stable, indicator of system integrity within the body by indexing the efficiency of information processing in the nervous system' [3]. By way of circumstantial support, the life-course stability of intelligence as a trait was cited, in addition to higher prior intelligence often being cited as a marker of 'cerebral reserve capacity'.

At a hand-waving level, we were pleased with this last formulation. The experience of suggesting it was that other scientists thought it to be plausible and worth exploring. But there were problems with it. We were aware that it was vague; we had neither tested nor even formulated system integrity in a sufficiently rigorous way so that it could be tested. Therefore, it was necessary to correct this. In preparing a later paper [4], we were urged to develop the concept further. We did so as follows:

'… the so-called "system integrity" hypothesis … posits that higher intelligence may be a marker for a general latent trait of a well-functioning body. That is, higher intelligence might be one aspect of a body that is generally "well-wired", and that responds more efficiently to environmental challenges or "allostatic load". Although advanced as a mechanism underlying the link between childhood IQ and mortality, system integrity might equally well account for associations observed between lower intelligence and health outcomes such as obesity, poorer self-rated health, and psychological distress. These outcomes – themselves risk factors for premature mortality – could reflect a body whose regulatory systems adapt less effectively to environmental challenges … the system integrity hypothesis has been little tested. In fact, it is still vague. It is based on the idea that there is a latent trait of optimal bodily functioning – the ability to respond well to environmental challenges with a return to equilibrium' [4].

Below, I describe some attempts to test the system integrity hypothesis, and ideas for some future attempts. Prior to that, I address two issues. First, I indicate that, although we thought we had come up with the system integrity idea ex novo, there was a precedent. Second, I explain why the system integrity hypothesis is not the same as the common cause hypothesis.

System Integrity: A Precedent

Several years after suggesting the system integrity hypothesis, I was re-reading Charles Spearman's magnum opus on intelligence differences, *The Abilities of Man* [5]. In the chapter on 'Mind and Body', Spearman considered the association between ill health and intelligence. Though the evidence was equivocal, he wrote, 'There is some other evidence, however, which tends more to support the old maxim, *mens sana in corpore sano*. The gifted children of Terman, for instance, showed on an average nearly 30 percent less "general weakness" than ordinary children. They also suffered less from "nervousness" and from headaches' (p. 399). Spearman then cited and discussed a 1920 study by Sandwick [6] who reported results on 423 high school students who had taken an intelligence test. The top and bottom 40 scorers' names were given to the school nurse who provided their health cards. Sandwick concluded that, 'the defects among the ablest group were not only fewer in number but less serious in character … the investigation adds something to the accumulating evidence that the child of good intellectual ability is also of good physical ability' (p. 202).

Spearman [5] found the results, 'startling' (p. 399). He went on, 'Doubt only remains as to the relation of cause and effect. Do the bodily ailments produce the lowering of *g* [general intelligence]? Or are the two ills only outward manifestations of some more deeply seated weakness?' (p. 399). From Spearman, this type of thinking is unsurprising. It was he who discovered that mental tests are positively correlated and who came up with the idea (and, to an extent, the statistical procedures) that this was because each was an indicator of a latent trait of general intelligence. And here he was expanding that same type of thinking that, if mental and physical capability were correlated, there might be some latent aspect of the body that shows variance and that these capabilities share some of it.

The System Integrity Hypothesis Is Not the Same as the Common Cause Hypothesis

It is useful if this issue is dealt with early in the paper, lest there be confusion or annoyance generated because the reader thinks the same idea is being peddled under two names. The common cause hypothesis may be traced to the work of Lindenberger and Baltes [7], who reported that sensory and cognitive functions were correlated in older people. Among other possible explanations they suggested that, 'according to the common cause hypothesis, negative age differences in both domains (sensory and cognitive) reflect an age-associated loss in the integrity of brain physiology. Age differences in intellectual and sensory functioning, then, are seen as the outcome of a third common factor or ensemble of factors, that is, aging changes in the physiological state of the brain' (p. 352).

Their findings were based on cross-sectional data, and longitudinal analyses – crucial for testing the hypothesis [8] – have not been numerous and have tended to find far weaker shared effects [9]. The common cause hypothesis was originally quite restricted in terms of the bodily systems it covered. For example, in their review, Li and Lindenberger [10] stated that, 'in late life, a common, biologically based factor is able to account for much of the age-related variance in sensory, sensorimotor, and intellectual functioning' (p. 781). However, other researchers have broadened this to include more physical functioning aspects of ageing [11, 12]. In including a broad range of bodily systems it is similar to the system integrity hypothesis.

The difference between the common cause and system integrity hypotheses is that the former concentrates on ageing effects (it posits correlated ageing slopes/trajectories across bodily systems), and the latter concentrates on the initial/optimal state of the systems (it posits correlated intercepts in early life prior to ageing effects). In making this distinction it echoes Hebb's [13] distinction between the first establishment of a complex brain function and the subsequent maintenance of that function. As stated in a neuro-computational model that addressed this distinction, 'Hebb argues that greater system integrity may be required for the initial establishment of a function than for the preservation of an already-established function' (p. 1030) [14].

Thus, the key data for testing the common cause hypothesis are longitudinal data collected in parallel across bodily systems. It does not remark on how individual differences in those systems should correlate in youth. The next section explains what the key data are for testing the system integrity hypothesis.

Testing the System Integrity Hypothesis

Clarity in Formulating 'System Integrity' Hypotheses

The system integrity hypothesis in cognitive epidemiology posits the following. There is a latent bodily trait of system integrity. There are individual differences in this trait. These differences underlie, to some extent, performance differences in complex bodily systems. Performance differences on various complex bodily systems will act as indicators of system integrity differences. This includes how effectively we meet cognitive and health challenges from the environment. The nature and causes of the bodily system differences are not yet known. In this last consideration, the position is not unlike that of the concept of cerebral reserve, which is another 'intuitively attractive concept' [15] where it has also been easier to point at potential markers of the concept than to reveal its mechanistic basis.

Given this formulation, the following must apply for there to be supporting empirical evidence for system integrity. First, there should be plausible marker traits for the latent trait of system integrity. That is, as with intelligence, there should be other differences for which an a priori case may be made that they are the indicators of some more general bodily efficiency. Second, each of these plausible marker traits for system integrity should be significantly associated with future health, illness and/or survival differences. In this first empirical test, the marker trait should be associated with health outcomes with which other indicator traits of system integ-

rity have been associated. Third, the marker traits should be significantly correlated – ideally in youth, at a time when each system is not affected by age-related changes or morbidity – such that better performance on one is associated with better performance on the other. That is, if the traits are both thought to be indicators for a more general latent trait of system integrity, then they should have significant covariance in their disease-free state, because it is their overlap that is the clue to their health relevance. Fourth, adjusting a system integrity marker's association with a health/illness/survival variable for differences in another system integrity marker should substantially attenuate or nullify the association. This also follows from the fact that the system integrity traits are thought to be indicators of a latent system integrity trait. Because it is their covariance, or overlap, that is the locus of the system integrity variance, then, when this variance is removed by adjusting one trait for variance in the other, the trait's association with health outcomes should substantially reduce. Keeping this set of rules in mind, we now examine some attempts to test the system integrity idea in cognitive epidemiology.

Speed of Information Processing

Reaction times are typically stated to assess speed of information processing, something which is thought to be fundamental with respect to brain efficiency, though the thought is moot [16]. Individual differences in people's means and variabilities in reaction time procedures are moderately highly correlated with higher-level cognitive abilities [17], and they are seen as possibly explanatory because of their simpler performance demands. Salthouse [18], especially, put processing speed integrity at the centre of his explanation for cognitive ageing across cognitive domains. He proposed a cognition-specific version of the common cause hypothesis, as follows: 'increased age in adulthood is associated with a decrease in the speed with which many processing operations can be executed and that this reduction in speed leads to impairments in cognitive functioning' (p. 403). There is longitudinal evidence that some ageing effects on cognition are domain-general [19], though Salthouse has in more recent writings down-played the 'master' explanatory role of processing speed and, instead, portrays processing speed [20, e.g. in his fig. 3.9, p. 91] as just one of the cognitive domains that is negatively affected by ageing.

Though their once-starring role in cognitive ageing might be waning, measures of processing speed were thought to be plausible markers of system integrity; they appear to assess some more basic processes than do complex cognitive tasks and in old age they relate to childhood cognitive functions [21]. Therefore, an attempt was made to test the system integrity hypothesis using differences in people's simple and 4-choice reaction times [22]. Reaction times – especially 4-choice reaction times – and their variabilities were associated with mortality, in this and other [23] studies. Reaction times and intelligence were significantly correlated: for example, the correlation between 4-choice reaction time mean and the Alice Heim 4 intelligence test part I was 0.49 [17, 22]. On adjusting the intelligence-mortality association for reaction times, the association was markedly attenuated and no longer significant.

Such a study has some valuable aspects. Reaction times are simpler in content than intelligence-type tests and perhaps less likely to be caught up in educationally- and socio-economically-related variance. They have been seen as more basic aspects of information processing in the brain, at a lower level of reduction than intelligence tests. The study [22] was done on middle-aged people followed into old age. Later work also found reaction times to be predictive of survival in younger adult samples [23]. Therefore, it was argued that reaction time's association with mortality might not just be the measure's picking up any age-related deterioration in processing efficiency; instead, reaction times might be somewhat trait-like indicators of processing efficiency. Evidence for the latter came from the finding that processing speed variables at age 70 are quite strongly associated with intelligence test scores almost 60 years earlier and, even more powerfully, that adjusting contemporaneous correlations between intelligence test scores and processing speed measures at age 70 for intelligence test scores at age 11 almost completely attenuated them [21].

Not only does reaction time have associations with mortality, and attenuate intelligence's associations with mortality, it also has effect sizes on mortality that are comparable or larger than several traditional risk factors [24]. Also, behavioural genetic research that has included both intelligence test scores and processing speed has found much shared genetic influence for the two [25]. So, does the reaction time evidence support system integrity? Possibly not. It seems likely that both intelligence tests and reaction time measures are just too similar: both assess cognitive function. Properly to assess the system integrity idea, one should have some more discrete markers, from more distant systems. Reaction time might simply be one of the underpinnings of intelligence differences: along the causal chain, so to speak, in the same narrow system, and not helping us to understand bodily health

any better. It is necessary to move further away from cognition to test the hypothesis more convincingly. Indeed, it might be argued that the more superficially dissimilar the system integrity markers, then the better the chance we have in thereby triangulating the underlying construct.

Physical Co-Ordination

Physical co-ordination seemed to provide a better test of the system integrity hypothesis than reaction time [4]. It is a complex, integrated process and yet generally considered to be distinct from cognitive ability. Physical co-ordination and intelligence test scores were available from childhood in the British birth cohorts of 1958 and 1970. At age 33, both cohorts assessed the following health outcomes: self-rated health, obesity, and psychological distress. It is a limitation of this study that the subjects were not old enough to have much mortality. The first two of the empirical demands of the system integrity hypothesis were met: the two markers correlated significantly in both cohorts (albeit modestly), such that more intelligent children tended to be better co-ordinated. Both markers were significant predictors of the health outcomes more than 20 years later. However, when adjusted for the other, each was still a significant predictor of the health outcomes, and the effect sizes were not attenuated. That is, both co-ordination and intelligence were significant predictors of these health outcomes, but they were also independent; their contribution to variance in health outcomes was not shared, and seemed not to be indicating some underlying common trait. These findings are interesting in themselves, but are not straightforwardly able to be accommodated in the system integrity formulation. The report suggested that multiple bodily systems might be used and that variance shared by them (a latent trait) should be looked to for association with health outcomes. Below, we shall see such an approach used with the concept of allostatic load but, next, we stay with physical capability.

Physical Strength

It should be stated first that there is as yet no adequate empirical test of physical strength and intelligence with regard to the system integrity hypothesis. However, there are some interesting, indicative data. Physical strength is often measured as grip strength. Lower intelligence and grip strength are associated with mortality in older people. Both decline with age. And the two show cross-sectional correlations in old age. A study based on the Lothian Birth Cohort 1921 (LBC1921) examined grip strength and non-verbal reasoning in parallel on three occasions from age 79 to 87 years [26]. Growth curve modelling was used to extract intercepts and slopes from each variable, in order to test whether there were lead-lag associations, which could indicate whether one might be driving ageing-related changes in the other. In fact, there were no associations between their slopes, and the intercept of one did not affect the slope of the other. What was found was that the two variables were correlated cross-sectionally. Therefore, although they were associated, they did not share ageing-related variance across the ninth decade, and one did not appear to cause age-related deterioration in the other.

In the paper, the following question was posed: 'Can the association between reasoning and grip strength within old age be traced back to childhood?' This is an intriguing possibility, for, if both are known to be associated with survival and they show cross-sectional correlations in old age, but not any reciprocal dynamic ageing association, then they might serve as markers of a lifelong trait of system integrity. The answer was unclear. In the LBC1921 cohort there were data on intelligence test scores from childhood, but not on grip strength. There was a high correlation between intelligence test scores in childhood and in old age, including up to age 87. However, there was no significant association between intelligence in childhood and grip strength in old age, suggesting that they might not have lifelong shared variance, which would be required by the system integrity hypothesis. There was some evidence from another study – the British 1946 birth cohort – that intelligence and grip strength might have shared origins, but this was equivocal, and the two did not correlate in middle age [27].

Fluctuating Asymmetry

Fluctuating asymmetry is a measure of the dissimilarity of two sides of the body. In humans, facial symmetry is often studied, and also other parts of body, such as fingers, wrists, ankles, ears, etc. The fundamental idea is that the achievement of symmetry is difficult, requires the co-ordination of many complex, interdependent developmental systems, and is an indicator of a system in good shape. It has also been debated whether – and the two are not exclusive – the attainment of symmetry reflects a good original blueprint/programme for development (system integrity?), or if symmetry is a record of the ability to respond to environmental perturbations which, in a less efficient system, might have been removed further from equilibrium and been left as asymmetrical.

Fluctuating asymmetry has many of the qualities looked for in an indicator of system integrity. It has the

above-mentioned theoretical orientation, as an indicator of bodily integrity. It has been associated with health and with intelligence, though not unequivocally. A meta-analysis found 14 samples with a total of 1,871 subjects, and concluded that people scoring higher on intelligence tests tended to be more symmetrical, with an effect size (*r*) between 0.12 and 0.20 [28]. In addition, it is not possible simply to include facial and bodily symmetry as indicating the same sets of influences. For example, childhood social status in men was associated with facial symmetry in old age; but this effect was not found in women, and not in men for bodily symmetry [29]. The suggestion was made that, 'bodily symmetry reflects the precision of molecular assembly and three-dimensional morphology … . By contrast, the arguably mostly soft-tissue symmetry indexed by facial symmetry appears more sensitive to environmental impacts and is linked to differential rates of decline in old age, rather than to more stable trait levels of ability' [29]. It will be informative to have studies that include both cognitive ability and symmetry (both types) measures and then follow up for morbidity and mortality.

Metabolic Syndrome

System integrity was intended as a source of variation that was shared by different bodily systems. Therefore, evidence that there is variance shared by different health-related phenotypes (other than trivially-obvious ones) is potentially valuable in pursuing the idea of system integrity. Relevant to this is work in cognitive epidemiology on the metabolic syndrome. This is a combination of the body's response to a glucose load, its adiposity (waist-hip ratio or body mass index), blood pressure, and lipid status. Each of these is under multiple influences, and each is under stress that tends to take values away from equilibrium. A good system might be viewed as one that can keep all of these at optimal levels.

Crucially, for system integrity, the metabolic syndrome also has three further characteristics. The elements are correlated and they form a latent trait when analysed using structural equation modelling formally to test whether a latent trait exists [30]. In longitudinal studies, lower prior cognitive ability is associated with a greater likelihood of developing the metabolic syndrome [30, 31]. Variance in the metabolic syndrome accounted for about a third of the cognition-cardiovascular disease mortality risk, though not for cognition all-cause mortality risk [30]. Of course, following this up requires better understanding of the causes of the metabolic syndrome and the cognition-metabolic syndrome association. And the metabolic syndrome concept is one construct in an even broader framework, in the more general concept of allostatic load, which is discussed below [32].

Genetic Correlation and Pleiotropy

Both cognitive ability and health differences show some degree of heritability. One source of shared phenotypic variation could lie in shared genetic causes. Such shared genetic causes could contribute to the mechanisms of bodily systems that are more or less generally robust. Such a possibility could be explored using both behavioural and molecular genetic approaches.

In a behavioural genetic study, the Generation Scotland: Scottish Family Health Study was used to estimate genetic correlations between cognitive ability and cardiovascular disease risk factors that were normally viewed as environmental in causation [33]. There were genetic correlations (in parentheses) between general cognitive ability and education (0.63), average income (0.45), smoking (0.45), and fruit and vegetable intake (0.23). That is, each of these variables was found to be partly heritable, and the genetic contribution to variance in them was shared to some extent with cognitive ability test scores. It is a long way from these associations to understanding the physiology of brighter, healthier and longer-living individuals, but the results do give pause before merely intuitively labelling influences as environmentally- or genetically-based causes. For example, in one of the studies on intelligence and metabolic syndrome, it was found that education was a mediator between the two [31]. However, these behaviour genetic results mean that it cannot merely be concluded that education is an environmental effect, as we have discussed elsewhere [34]. Ideally, a behaviour genetic study should include a large sample of mono- and dizygotic twins with information on cognitive ability in youth and who have then been followed up until most of the sample has died, with health and illness information available in the interim. That would be a rare dataset, but it is a worthwhile exercise always to ask what an ideal study would look like.

Genome-wide association analyses have not provided many low-hanging fruit (single mutations with large or even modest effect sizes) for complex traits like cognitive ability. However, new methods of analysis that use all the information in dense genetic arrays that include hundreds of thousands of single-nucleotide polymorphisms have been able to account for a substantial minority of the variance in intelligence [35]. It is only a matter of time, therefore, before this trait is joined in multivariate genome-wide analyses to ask whether the genetic risk of

lower intelligence is associated with the genetic risk for other physical and mental disorders with which it is linked. Given their progress in genome-wide studies – and their links with and relevance to prior cognitive ability and cognitive ageing – the first among these are likely to be type 2 diabetes, cardiovascular disease, and mood disorders. Will that help to test the system integrity hypothesis? It might, if there are identifiable shared genetic variants. But caution must be raised, because it is typical for complex traits to have many genetic contributions that are very small in effect size. That is, even if a shared genetic signal emerges, it is possible that individual allelic contributions to that signal are so small that they could be unidentifiable.

Beyond genetic variants per se (such as single-nucleotide polymorphisms or even copy number variants) it should be borne in mind that epigenetic influences (e.g. those on gene methylation) could also be a source of shared cognitive-health associations. It is already known, from animal models, that regulation of gene expression by methylation (caused, for example, by differences in maternal behaviour) can have an effect on systems that are involved in health and brain function [36]. Methylation effects can occur from very early in human development, and are a potential source of system integrity differences.

Conclusions

What Do We Mean by 'System Integrity'

The original notion of system integrity was that it meant the processing quality of the human machine as it came out of the factory door. The idea was that there was some link in quality between the various complex systems at this early stage, perhaps because the blueprint, the materials or the fabrication procedures – or some combination of all of these – was better in some than in others. This initial 'as-perfect-as-possible' system integrity refers to an almost impossible-to-measure state, given what we know about, for example, foetal development and how that influences chronic diseases in later life, and how epigenetic (e.g. methylation) effects can work in very early development. So, will system integrity be an elusive concept, because all assessments of intelligence, for example, will always be indicators of both it and the tribulations that the system has already suffered? Perhaps not entirely, if part of the answer lies in genomic differences. Behaviour genetic and molecular genetic studies will appear that ask whether the phenotypic correlations between intelligence and health measures have any genetic basis. Some already predict that this is the case, and such authors view intelligence as one aspect of a more general fitness factor that is a signal for sexual selection [37, 38].

But it is still not as straightforward as that. Take, for example, the common variation in the gene for apolipoprotein E, *APOE*, whereby about a quarter of people have an e4 allele. Possession of this allele is associated with, for example, cardiovascular outcomes and late-onset Alzheimer's disease and accelerated cognitive ageing, though not childhood intelligence. But the point here is that these genetic differences might be present from conception, but are, arguably, part of the 'ongoing system repair' rather than 'original system integrity'. Of course, they are knowable from birth. This means that we might be in a position of knowing, from genetic status that, although there are no measurable phenotypic differences early on, some systems are predisposed to less good repair (or response to allostatic load more generally) subsequently. To the extent that the system integrity idea states that there should be measurable phenotypes of this latent trait from early in the life course, such a state of affairs would not be included within it.

Is System Integrity a 'Theoretical Soup Stone'?

In science we can invoke concepts that are in essence illusory: they ultimately do not explain or predict, even though they appeared at one time to have such power. This is the idea of the soup stone; it comes from the tale that to make good soup one needs this stone, though it also helps to have a good stock, vegetables, seasoning, and meat (if desired). This was memorably applied to the concept of human cognitive processing 'resources' [39]. It has occurred to me that, when we understand the factors and mechanisms that afford one person's meeting brain pathology with less cognitive decrement than another person, we might be able to shed the concept of cognitive 'reserve' [15], or maybe we shall use it as a decorative carrying basket for a collection of the truly explanatory factors.

It is possible that there are some 'initial conditions' – differences across bodily systems that share variance – that explain the covariance between early life cognitive ability and later health. The point here is that when we know the causes and mechanisms of these, we might be able to slough off the holding concept of system integrity. Its usefulness, then, will have been that it was a place marker for somewhere we intended to look for explanation, and where we were pointing to others to investigate.

Jingling and Jangling

We should be careful that system integrity is not just a new form of words for something that is already out there under another name. It is scientific bad practice to make neologisms where an existing concept is already doing the same job. This practice has been rife for so long in psychology that it long ago was given the name of the 'jangle fallacy', and was described as being the scientific error of having, 'Two separate words or expressions covering in fact the same basic situation, but sounding different, as though they were in truth different' [40, p. 64].

System integrity is not the same as cognitive reserve, for example, because the latter applies to cognitive changes after the onset of brain pathology. Similarly, as explained above, it is not the same as the common cause hypothesis of cognitive ageing, because this refers to possible causes of shared age-related changes across systems, not to how initial bodily conditions across systems might anticipate later health and survival.

System integrity is closer to the idea of allostatic load – or 'multisystem biological risk', which can already be detected as a general latent trait in young adults – which combines (including formally statistically) fitness across cortisol, hormones, metabolism, inflammation, blood pressure, and heart performance [32]. The authors suggested that, 'such a metafactor model of AL [allostatic load] may be a particularly useful tool in efforts to assess the multiple physiological pathways through which factors such as socio-economic status or exposure to chronic stress impact health' (p. 471). And intelligence, of course. The researchers on allostatic load emphasise the cross-system covariance that is at the heart of the system integrity ideas: 'surprisingly little attention has been paid to the health impacts of the co-occurrence of physiological dysregulation across multiple systems' (p. 463). And system integrity is also akin to the idea of a general fitness, '*f*', factor suggested by others [37, 38]. This general fitness factor is conceptualized by the authors as being caused by 'mutation load' [38].

Likely Same Effects/Causes for All Types of Death?

One of the problems for explanation in cognitive epidemiology is the wide range of causes of mortality [1, 2] and other health outcomes [38, 41] with which intelligence differences are associated. Can a single cause or set of causes possibly explain such different morbidities and mortalities? This is a good point at which to remind readers that system integrity was only ever suggested to be one of a number of non-exclusive explanations for cognitive ability-illness/mortality associations; it was not expected that it might do all the work. Nevertheless, the allostatic load [32] and fitness factor [38] accounts are conceptualized as broad in their ranges of influence.

Another general explanation for the intelligence-survival association has been suggested in the form of 'personal characteristics, the habits, tendencies, and behaviours that lead to academic success' [42]. This was a result of the finding that rank in high school class mediated the association between IQ and survival. However, the personality characteristics that were invoked to 'explain' the intelligence-survival association were likened to the personality trait of conscientiousness which, when it has been examined alongside intelligence, adds independent variance to the prediction of survival rather than accounting for the intelligence-survival association [43].

If progress is to be made in increasing the utility of the system integrity construct in cognitive epidemiology, there should be: additional plausible markers suggested for the construct; the expansion to additional types of study, including multivariate, health-focussed behaviour- and molecular-genetic studies, and a proper evaluation of system integrity in the context of related constructs. After all that, one cannot guarantee that the now-attractive construct of system integrity will not evaporate like Scotch mist.

Acknowledgements

The work was undertaken in The University of Edinburgh Centre for Cognitive Ageing and Cognitive Epidemiology, part of the cross-council Lifelong Health and Wellbeing Initiative (G0700704/84698). Funding from the Biotechnology and Biological Sciences Research Council (BBSRC), Engineering and Physical Sciences Research Council (EPSRC), Economic and Social Research Council (ESRC) and Medical Research Council (MRC) is gratefully acknowledged.

References

1 Calvin CM, Deary IJ, Fenton C, Roberts B, Der G, Leckenby N, Batty GD: Intelligence in youth and all-cause mortality: systematic review with meta-analysis. Int J Epidemiol 2011;40:626–644.

2 Deary IJ: Cognitive epidemiology: its rise, its current issues, and its challenges. Peronal Individ Diff 2010;49:337–343.

3 Whalley LJ, Deary IJ: Longitudinal cohort study of childhood IQ and survival up to age 76. BMJ 2001;322;819–822.

4 Gale CR, Batty GD, Cooper C, Deary IJ: Psychomotor co-ordination and intelligence in childhood and health in adulthood: testing the system integrity hypothesis. Psychosom Med 2009;71:675–681.
5 Spearman C: The Abilities of Man. London, Macmillan, 1927.
6 Sandwick RL: Correlation of physical health and mental efficiency. J Educ Res 1920;1: 199–203.
7 Lindenberger U, Baltes PB: Sensory functioning and intelligence in old age: a strong connection. Psychol Aging 1994;9:339–355.
8 Hofer SM, Sliwinski MJ: Understanding ageing: an evaluation of research designs for assessing the interdependence of ageing-related changes. Gerontology 2001;47:341–352.
9 Sternang O, Jonsson B, Wahlin A, Nyberg L, Nilsson L-G: Examination of the common cause account in a population-based longitudinal study with narrow age cohort design. Gerontology 2010;56:553–563.
10 Li KZH, Lindenberger U: Relations between aging sensory/sensorimotor and cognitive functions. Neurosci Biobehav Rev 2002;26: 777–783.
11 Christensen H, Mackinnon AJ, Korten A, Jorm AF: The 'common cause hypothesis' of cognitive aging: evidence for not only a common factor but also specific associations of age with vision and grip strength in a cross-sectional analysis. Psychol Aging 2001;16: 588–599.
12 Aihie Sayer A, Osmond C, Briggs R, Cooper C: Do all systems age together? Gerontology 1999;45:83–86.
13 Hebb DO: The Organization of Behavior. New York, Wiley, 1949.
14 Varier S, Kaiser M, Forsyth R: Establishing, versus maintaining, brain function: a neurocomputational model of cortical reorganization after injury to the immature brain. J Int Neuropsychol Soc 2011;17:1030–1038.
15 Stern Y: Cognitive reserve. Neuropsychologia 2009;47:2015–2028.
16 Deary IJ: Looking Down on Human Intelligence. Oxford, Oxford University Press, 2001.
17 Deary IJ, Der G, Ford G: Reaction times and intelligence differences: a population-based cohort study. Intelligence 2001;29:389–399.
18 Salthouse TA: The processing speed theory of adult age differences in cognition. Psychol Rev 1996;103:403–428.
19 Tucker-Drob E: Global and domain-specific changes in cognition throughout adulthood. Dev Psychol 2011;47:331–343.
20 Salthouse TA: Major Issues in Cognitive Ageing. Oxford, UK, Oxford University Press, 2010.
21 Deary IJ, Johnson W, Starr JM: Are processing speed tasks biomarkers of cognitive ageing? Psychol Aging 2010;25:219–228.
22 Deary IJ, Der G: Reaction time explains IQ's association with death. Psychol Sci 2005;16: 64–69.
23 Shipley BA, Der G, Taylor MD, Deary IJ: Cognition and all-cause mortality across the entire adult age range: health and lifestyle survey. Psychosom Med 2006;68:17–24.
24 Roberts BA, Der G, Deary IJ, Batty GD: Reaction time and established risk factors for total and cardiovascular disease mortality: comparison of effect estimates in the follow-up of a large, UK-wide, general-population based survey. Intelligence 2009;37:561–566.
25 Luciano M, Wright MJ, Geffen GM, Geffen LB, Smith GA, Martin NG: A genetic investigation of the covariation among inspection time, choice reaction time, and IQ subtest scores. Behav Genet 2004;34:41–50.
26 Deary IJ, Johnson W, Gow AJ, Pattie A, Brett CE, Bates T, Starr JM: Losing one's grip: a bivariate growth curve model of grip strength and non-verbal reasoning from age 79 to age 87 years in the Lothian Birth Cohort 1921. J Gerontol B Psychol Sci Soc Sci 2011;66:699–707.
27 Kuh D, Cooper R, Hardy R, Guralnik J, Richards M: Lifetime cognitive performance is associated with midlife physical performance in a prospective national birth cohort study. Psychosom Med 2009;71:38–48.
28 Banks GC, Batchelor JH, McDaniel MA: Smarter people are (a bit) more symmetrical: a meta-analysis of the relationship between intelligence and fluctuating asymmetry. Intelligence 2010;38:393–401.
29 Hope D, Bates T, Penke L, Gow AJ, Starr JM, Deary IJ: Symmetry of the face in old age reflects childhood social status. Econ Hum Biol (E-pub ahead of print).
30 Batty DG, Gale CR, Mortensen LH, Langenberg C, Shipley MJ, Deary IJ: Premorbid intelligence, the metabolic syndrome and mortality: the Vietnam Experience Study. Diabetologia 2008;51:436–443.
31 Richards M, Black S, Mishra G, Gale CR, Deary IJ, Batty DG: IQ in childhood and the metabolic syndrome in middle age: extended follow-up of the 1946 British Birth Cohort study. Intelligence 2009;37:567–572.
32 Seeman, T, Gruenwald T, Karlamangla A, Sindey S, Liu K, McEwen B, Schwartz J: Modeling multisystem biological risk in young adults: the coronary artery risk development in young adults study. Am J Hum Biol 2010; 22:463–472.
33 Luciano M, Batty GD, McGilchrist M, Linksted P, Fitzpatrick B, Jackson C, Pattie A, Dominiczak AF, Morris AD, Smith BH, Porteous D, Deary IJ: Shared genetic aetiology between cognitive ability and cardiovascular disease risk factors: Generation Scotland's Scottish Family Health Study. Intelligence 2010;38:304–313.
34 Deary IJ, Johnson W: Intelligence and education: causal perceptions drive analytic processes and therefore conclusions. Int J Epidemiol 2010;39:1362–1369.
35 Davies G, Tenesa A, Payton A, Yang J, Harris SE, Liewald D, et al: Genome-wide association studies establish that human intelligence is highly heritable and polygenic. Mol Psychiatry 2011;16:996–1005.
36 Feil R, Fraga MF: Epigenetics and environment: emerging patterns and implications. Nat Rev Genet 2012;13:97–109.
37 Penke L, Denissen JJA, Miller GF: The evolutionary genetics of personality. Eur J Pers 2007;21:549–587.
38 Arden R, Gottfredson LS, Miller G: Does a fitness factor contribute to the association between intelligence and health outcomes? Evidence from medical abnormality counts among 3654 US veterans. Intelligence 2009; 37;581–591.
39 Navon D: Resources – a theoretical soup stone? Psychol Rev 1984;91:216–234.
40 Kelley L: Interpretation of Educational Measurements. Yonkers/NY, World, 1927.
41 Der G, Batty DG, Deary IJ: The association between IQ in adolescence and a large range of health outcomes at 40 in the US National Longitudinal Study of Youth. Intelligence 2009;37:573–580.
42 Hauser RM, Palloni A: Adolescent IQ and survival in the Wisconsin Longitudinal Study. J Gerontol B Psychol Sci Soc Sci 2011; 66B:i91–i101.
43 Deary IJ, Batty GD, Pattie A, Gale CG: More intelligent, more dependable children live longer: a 55-year longitudinal study of a representative sample of the Scottish nation. Psychol Sci 2008;19:874–880.